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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/373,182	08/12/1999	KIM MCCLURE	PC10240A	2284

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EXAMINER	
WEBER, JON P	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 04/16/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/373,182	Applicant(s) MCCLURE ET AL.	
	Examiner Jon P. Weber, Ph.D.	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-81* is/are pending in the application.

4a) Of the above claim(s) *1-59 and 62-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-61 and 80-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Status of the Claims

The response with amendments filed 31 January 2002 has been received and entered. Claims 1-81 have been presented for examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

This application contains claims 1-59 and 62-79 drawn to an invention nonelected with traverse in Paper No. 7, filed 03 May 2001. A complete reply to the final rejection **must** include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Specification

The communication filed 31 January 2002 is not fully responsive to the Office communication mailed 11 July 2001 for the reason(s) set forth on the Notice To Comply With The Sequence Rules or CRF Diskette Problem Report faxed to applicant on 08 March 2002. Applicant **must** comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) for the response to this Office action to be complete, although the examination of this application on the merits can proceed at this time.

Claim Rejections - 35 USC § 112

Claims 60-61 and new claims 80-81 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain compounds which exhibit 100-fold or 500-fold selectivity for TACE over MMP1, does not reasonably provide enablement for any compound which exhibits said selectivity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

It is argued that an assay is set forth in the claims and disclosure for the desired degree of selectivity coupled with the large number of known inhibitors of TACE is sufficient to establish enablement.

The claims as amended now recite a specific degree of selectivity, 100-fold or 500-fold for TACE over MMP1. The specification at Table A provides evidence for specific compounds which can meet these claims. However, more compounds fail to meet these limitations than meet them. This suggests that there is a high degree of unpredictability in the selection of suitable inhibitors. The lack of measurement of inhibition of both enzymes in prior art references was discussed in the Office action of 11 July 2001. This renders it difficult to predict from the observation of TACE inhibition that a given inhibitor will exhibit the required selectivity. There are no clear structural elements or requirements that have been described in the instant disclosure that would lead a person of ordinary skill in the art to select a particular inhibitor. That is the disclosure does not provide any general degree of guidance on the selection of desired inhibitors that meet the claimed inhibitors.

The response argues that 35 U.S.C. § 112, first paragraph, permits an artisan to present claims of essentially limitless breadth so long as the specification provides one with the ability to test any particular embodiment which is encompassed by the material limitations of a claim and thereby distinguish between those embodiments which meet the functional limitations from those embodiments which don't. This argument is not entirely without merit. However, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. This 'make and test' position is inconsistent with the decisions in *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), *Amgen v. Chugai Pharmaceuticals Co. Ltd.*, 13 USPQ2d, 1737 (1990), and *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988). *In re Wands* stated that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims.

All of these factors were addressed in the initial rejection. Breadth alone is not the issue, however. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific

law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Having established the breadth of the claims, *Wands* now requires that one consider the number of working examples presented in the instant specification. It is noted that there specific examples in the instant specification which have the claimed degree of selectivity. Since there are only limited working examples, then one must consider the general guidance is provided by the instant specification and the prior art of record. The instant specification provides absolutely no guidance as to which structural elements or features are essential for the functional selectivity as claimed. Further, there is no functionally and structurally analogous inhibitors which have been identified in the prior art for which this information is known and could be extrapolated to the instant inhibitors by analogy. In conclusion, the instant claims encompass a vast, almost limitless, number of inhibitors and yet the instant specification provides limited specific working examples and no general guidance that would permit and artisan to practice the invention commensurate with the scope of the instant claims.

The response's argument is based upon a premise that the standard under 35 U.S.C. § 112, first paragraph, is that of making a subject inhibitor and testing to see if it obtains the desired biological activity and properties. This is a position that has been routinely dismissed by the courts, as shown by those decisions cited above.

Further, *In re Wands* determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to specific inhibitors and the instant specification does not provide a description of a repeatable process of producing a selective inhibitor. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work

that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination the structural elements which are required for the claimed selectivity. It is this additional characterization of the properties that is required in order to obtain the functional and structural data needed to permit one to produce an inhibitor which meets both the functional requirements of the instant claims that constitutes undue experimentation.

With regard to the propriety of specifically considering the decisions of *In re Fisher*, *Amgen Inc. v. Chugai*, and *In re Wands* to the exclusion of the plurality of decisions cited by Applicant in determining the patentability of the instant claims, Applicant is encouraged to review the discussion of 35 U.S.C. § 112, first paragraph in a recent CAFC decision, *Genentech, Inc. v. Novo Nordisk*, 42 USPQ2d, 100 (CAFC 1997), in which these three decisions were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the court because they show that the judicial interpretation of the first paragraph of 35 U.S.C. § 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a **reasonable expectation** that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are **more likely to work that not** without actually making and testing them then the instant application does not support the breadth of the claims. In the instant case it is highly improbable that any inhibitor of TACE will more likely than not perform in the manner disclosed, and the instant specification does not provide the guidance needed to predictably alter

that inhibitor with any reasonable expectation that the resulting inhibitor will function as an selective inhibitor for TACE over MMP1.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P. Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone numbers for

the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jon P. Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
April 12, 2002